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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/529,130	06/22/2000	MICHAEL JOHN DUGGAN	1581.0580000	2901

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EXAMINER
KAM, CHIH MIN

ART UNIT	PAPER NUMBER
1653	18

DATE MAILED: 11/26/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/529,130	DUGGAN ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-16,18-47,50-54 and 57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-16,18-47,50-54 and 57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *16* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Claims

1. Claims 1, 4-16, 18-47, 50-54 and 57 are pending.

Applicants' amendment filed on September 10, 2002 (Paper No. 17) is acknowledged, and applicants' response has been fully considered. Claims 1, 20-23, 32-37, 39-43, 46, 47, 51, 52, 54 and 57 have been amended, claims 2, 3, 48, 49 and 58-62 have been cancelled. Claim 57, which originally was restricted as a non-elected claim, has been requested by applicant to rejoin with other examined claims. Upon reconsideration, claim 57 will be rejoined with other claims under examination. Thus, claims 1, 4-16, 18-47, 50-54 and 57 are examined.

Rejection Withdrawn

Claim Rejections - 35 USC § 112

2. The previous rejection of claims 1-16, 18-54 and 58-61, under 35 U.S.C. §112, first and second paragraphs, is withdrawn in view of applicants' amendment to the claim, applicants' cancellation of the claim, and applicants' response at pages 8-22 in Paper No. 17.

Claim Rejections - 35 USC § 102

3. The previous rejection of claims 1-2, 4-16, 20-41, 44-48 and 50-54 under 35 U.S.C. 102(b) as being anticipated by Foster *et al.* (WO 96/33273), is withdrawn in view of applicants' amendment to the claim, applicants' cancellation of the claim, and applicants' response at pages 22-30 in Paper No. 17.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claim 57 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of alleviating pain by administering to a subject in need thereof an agent comprising a galactose-binding lectin, a L chain of a clostridial toxin or its functional fragment, and a translocation domain of a clostridial toxin, wherein the three components are linked together, does not reasonably provide enablement for a method of preventing (not even occur at the first time) pain by administering the agent to the subject. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claim 57 encompasses a method of alleviating or preventing pain by administering an agent comprising a galactose-binding lectin, a L chain of a clostridial toxin or its functional fragment, and a translocation domain of a clostridial toxin, wherein the three components are linked together. The specification indicates an agent comprising a galactose-binding lectin or a modified galactose-binding lectin, a L chain of a clostridial toxin or its functional fragment, and a translocation domain of a clostridial toxin, wherein the three components are linked together, can reduce and prevent the transmission of pain signals from nociceptive afferents to projection neurons (page 4, line 17-page 5, line 10; page 9, line 28-page 10, line 33). There are no indicia that the present application enables the full scope in view of the method of alleviating or preventing pain using the agent as discussed in the stated rejection. The present application provides no indicia and no teaching/guidance as to how the full scope of the claim is enabled. The factors considered in determining whether undue experimentation is required, are

summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breath of the claims, the absence of working examples, the state of the prior art and relative skill of those in the art, the unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breath of the claims:

The breath of the claim is broad and encompasses using the agent to prevent pain which is not adequately described or demonstrated in the specification.

(2). The absence of working examples:

There are no working examples indicating the agent can prevent pain, Example 9 merely shows ExL-LH_N/A has analgesic property.

(3). The state of the prior art and relative skill of those in the art:

The prior art (Foster *et al.*, WO 96/33273) indicates an agent comprising LH_N and a lectin can reduce the transmission of pain signals from nociceptive afferents to projection neurons (page 7, lines 15-17). However, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on how to monitor pain which is prevented to occur to be considered enabling for variants.

(4). The amount of direction or guidance presented and the quantity of experimentation necessary:

Claim 57 is directed to a method of alleviating or preventing pain by administering an agent comprising a galactose-binding lectin, a L chain of a clostridial toxin or its functional fragment, and a translocation domain of a clostridial toxin, wherein the three components are

linked together. The specification has only indicated the agent can be used for the treatment of pain (page 5, lines 5-7; Example 9). However, the specification fails to provide any example of using the agent for preventing pain. Moreover, the specification has not shown the treating conditions for preventing pain, nor has indicated how to monitor pain which is being prevented to occur. There are no working examples indicating such methods. Furthermore, the specification does not provide any specific guidance as to how to prevent pain as well as how the effect of the agent on pain being monitored if pain is prevented to occur. Since the specification fails to provide sufficient guidance how to prevent pain using the agent, it is necessary to have additional guidance as to how to carry out the experimentation for assessing the effect.

(5). Predictability or unpredictability of the art:

The claim encompasses preventing pain by administering the agent, however, the conditions for preventing pain are not described in the specification, and the invention is highly unpredictable regarding the outcome of the treatment.

(6). Nature of the Invention

The scope of the claim includes preventing pain, but the specification does not show how pain is being prevented. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broad, while the working example does not demonstrate the claimed invention, and the guidance and the teaching in the specification is limited, therefore, it is necessary to have additional guidance and to carry out further experimentation to assess the outcome of the treatment using the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1, 4-12, 14, 20-41, 44-47, 50-54 and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Foster *et al.* (WO 96/33273) taken with Sharon *et al.* (The FASEB Journal 4, 3198-3208 (1990)).

Foster *et al.* teach an agent containing lectin (page 13, lines 9-13) as the targeting moiety (TM) and a modified clostridial neurotoxin such as LH_N (including L-chain and its functional fragment, claims 1, 24-31, 35, 39, 46, 50), the clostridial neurotoxin having H_C chemically modified to reduce its ability to bind the receptor (claims 20-23, 36), and a hybrid molecule of a modified heavy chain (H_C being modified) of a clostridial toxin with a light chain of a different clostridial toxin (page 13, line 18-page 14, line 19; claims 32-34) can be obtained by covalently attachment of a TM to a modified clostridial neurotoxin using linkage including one or more

spacer regions (page 14, lines 1-9; claim 37, 40, 47) or can be expressed recombinantly as a fusion protein (page 14, line 29-page 15, line 4; claim 38, 41, 50). This agent can bind to a binding site on the surface of sensory neurons (page 12, lines 25-28) and reduce or preferably prevent the transmission of pain signals from nociceptive afferents to projection neurons (page 7, lines 15-17; claims 44-45), therefore it can be used for controlling the transmission of sensory information or pain signals from a nociceptive afferent to a projection neuron (claims 51-54 and 57). However, Foster *et al.* do not disclose using a specific lectin such as galactose-binding lectin in preparing the agent. Sharon *et al.* teach certain oligosaccharides such as complexed type oligosaccharides with terminal galactose residues can act as multivalent ligands that cross-link and precipitate galactose or N-acetylgalactosamine specific lectins such as soybean agglutinin, or those of different Erythrina species (page 3200, right column; Table 1; claims 4-12), and the S-type lectins in animals that have a specificity for β-galactosides (page 3198, right column; claim 14). At the time of invention was made, it would have been obvious to one of ordinary skill in the art to make the agent taught by Foster *et al.* and to use the specific lectin such as galactose-binding lectin taught by Sharon *et al.* because the galactose-binding lectins are widely available in legume plants (see Table 1 of Sharon *et al.*) and can serve as a cell-recognition molecule for the agent. Thus, the combined references result in the claimed invention and were, as a whole, prima facie obvious at the time the claimed invention was made.

6. Claims 13, 15, 16, 18, 19, 42 and 43 are rejected because they are dependent from a rejected claim.

Conclusion

7. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, Ph. D. can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. CMK
Patent Examiner

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November 21, 2002

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